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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/604,876	06/28/2000	Mercy M. Davidson	0575/56614/JPW/JML/HA	6365

7590 07/12/2005

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/604,876	DAVIDSON, MERCY M.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,8,9 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3-5,8,9 and 12* is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/29/03; 11/13/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

An amendment was received and entered on 4/25/05.

Claims 1, 3-5, 8, 9, and 12 remain pending in the application and are under consideration in this Office Action.

At page 6 of the response, Applicant asserts that in the interview of 1/18/05 agreement was reached as to the allowability of claim 1 as currently amended. The Examiner does not concur with this assertion.

Rejections Withdrawn

The rejection of claim 1 under 35 USC 112, first paragraph for lack of adequate written description is withdrawn in view of Applicant's amendments requiring the expression of beta myosin heavy chain, connexin-43, and desmin.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "obvious" in claim 1 is a relative term which renders the claim indefinite. The term "obvious" is not defined by the claim, the specification does not provide a

standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The parameter of voltage-activated conductances is rendered indefinite by the term "obvious".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 stands rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (In Vitro Cellular and Developmental Biology 27(1): 63-74, 1/1991).

Claim 1 is a product-by-process claim drawn to an immortalized human undifferentiated cardiomyocyte cell line produced by a particular process. The process requires fusing a post-mitotic primary non-immortalized human cardiomyocyte obtained from adult human heart tissue, wherein the cardiomyocyte has fused with a human fibroblast that has been treated with ethidium bromide, lacks mitochondrial DNA, and comprises a replicable vector expressing SV40 large T antigen. The claim requires that the cell line must express SV-40 large T-antigen, beta myosin heavy chain, connexin-43, and desmin. The claim recites the functional characteristic of "does not exhibit obvious voltage-activated conductances in whole cell voltage-clamp recordings".

MPEP 2113 states that product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by these steps. The clear structural requirements of the instantly claimed product are that it comprises a replicable

vector expressing SV40 large T antigen, it expresses beta myosin heavy chain, connexin-43, and desmin, and it contains no fibroblast mitochondrial DNA. The functional limitation "immortalized" is clear to one to skill in the art and breathes life and meaning in to the claim. In contrast, the preamble phrase "undifferentiated cardiomyocyte" carries little weight. The term "cardiomyocyte" by itself might imply certain structural and functional characteristics that would breathe life and meaning into the claim, however it is unclear what are the minimum requirements that must be met for a cell to be considered an "undifferentiated" cardiomyocyte. For example, it is unclear what markers would need to be expressed, and what physiological characteristics would have to be apparent. So, "undifferentiated cardiomyocyte" is given little weight. Also, the structural and functional consequences of fusion with a fibroblast are unclear, other than that the claimed product must comprise a replicable vector that expresses SV-40 large T antigen, and must also express beta myosin heavy chain, connexin-43, and desmin. Finally, the functional limitation of "does not exhibit obvious voltage-activated conductances in whole cell voltage-clamp recordings" is considered to be inherent in the structure of the claimed cell.

As a result, the claimed cell line would be anticipated by any immortalized human cell line comprising a replicable vector that expresses SV-40 large T antigen, and that expresses beta myosin heavy chain, connexin-43, and desmin.

Wang taught a dedifferentiated human fetal cardiac myocyte cell line designated W1 that carries an expression vector encoding SV40 T antigen (pRSVTAg). See abstract; page 67, column 2, last complete sentence; and page 73, column 2, last

paragraph. This cell line is considered to be immortalized because it was maintained in culture for one year. See abstract. This immortalization is considered by Wang to be evidence that the cells express T antigen. Wang taught that the pRSVTAg vector appeared to be integrated into cellular chromosomal DNA. See page 73, column 1, lines 5-11. This ensures that the vector is replicable. The cell line has a profile of immunoreactivity with 15 different antibodies against cardiomyocyte and non-cardiomyocyte antigens that is identical to the immunoreactivity profile of fetal cardiac myocytes. See Table 2 on page 69. Because the W1 cell line is disclosed as an undifferentiated cardiomyocyte that expresses cardiomyocyte markers, the Office considers the expression of cardiomyocyte markers such as connexin-43, beta myosin heavy chain, and connexin-43 to be inherent in the W1 cell line absent evidence to the contrary.

The Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See Ex parte Phillips, 28 USPQ 1302, 1303 (BPAI 1993), In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ2d 1922, 1923 (BPAI 1989). In this case the undifferentiated cell line of Wang is derived from a cardiomyocyte, expresses SV40 T antigen, and has a

profile of immunoreactivity that is identical to the immunoreactivity profile of fetal cardiac myocytes, suggesting that expresses cardiomyocyte markers inherently.

Response to Arguments

Applicant's arguments filed 11/12/04 have been fully considered but they are not persuasive. Applicant asserts at page 9 of the response that the W1 cell line of Wang does not express beta myosin heavy chain, connexin-43, and desmin. The W1 cell line is identified by Wang as a dedifferentiated cardiomyocyte. Wang also shows that the W1 line has a profile of immunoreactivity with 15 different antibodies against cardiomyocyte and non-cardiomyocyte antigens that is identical to the immunoreactivity profile of fetal cardiac myocytes. See Table 2 on page 69. In light of this information, the Office considers expression of cardiomyocyte markers to be inherent in the W1 absent evidence to the contrary. Applicant has provided no evidence that the cell line of Wang does not express beta myosin heavy chain, connexin-43, and desmin.

Applicant asserts at page 9 of the response that the W1 cell line differs from the claimed cell line because the claimed cell line is derived from an adult human cardiomyocyte, whereas the W1 line is derived from a fetal cardiomyocyte. This is unpersuasive because it is unclear that derivation from a fetal cardiomyocyte would lead to a structurally and functionally different cell than that which is claimed. The instant specification teaches derivation of the cardiomyocyte cell lines from both fetal and adult cardiomyocytes (see page 19, lines 38-40) and discloses that the cells obtained by the recited method steps had the same growth properties regardless of whether they originated from fetal or adult cardiomyocytes. Thus the available evidence suggests

that immortalized undifferentiated human cardiomyocyte cell lines derived from fetal cardiomyocytes are indistinguishable from those derived from adult cardiomyocytes.

At pages 9 and 10 of the response, Applicant argues that the W1 cell line is distinguishable from the claimed cell lines because it is morphologically different and has a different doubling time. Applicant relies for support on the declaration of Dr. Mercy Davidson (filed 5/18/2004) and considered in the Action of 8/11/04). This argument is unpersuasive because the claims recite no limitations regarding morphology or doubling time, and are broad enough to encompass the W1 cell line.

For these reasons the rejection is maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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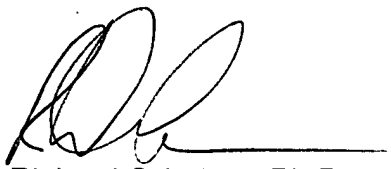

Richard Schnizer, Ph.D.